



DOCK8 gene

dedicator of cytokinesis 8

Normal Function

The *DOCK8* gene provides instructions for making a member of the DOCK family of proteins. The proteins in this family act as guanine nucleotide exchange factors (GEFs). GEFs turn on (activate) proteins called GTPases, which play an important role in chemical signaling within cells. Signaling stimulated by DOCK family proteins are typically involved in the arrangement of the structural framework inside cells (the cytoskeleton). By controlling the shape of the cytoskeleton, DOCK family proteins play a role in cell structure and movement (migration).

The DOCK8 protein is found most abundantly in cells of the immune system. DOCK8 plays a critical role in the survival and function of several types of immune system cells, including T cells, NK cells, and B cells. T cells and NK cells recognize and attack foreign invaders, such as viruses, to prevent infection. B cells produce proteins called antibodies, which attach to foreign particles and germs and mark them for destruction.

Through its function as a GEF, the DOCK8 protein helps maintain the structure and integrity of T cells and NK cells. It also aids in the migration of these immune system cells to sites of infection, particularly the skin. DOCK8 is also involved in chemical signaling pathways that stimulate B cells to mature and produce antibodies. DOCK8 is also involved in the normal development and survival of other types of immune system cells.

Health Conditions Related to Genetic Changes

autosomal recessive hyper-IgE syndrome

At least 110 mutations in the *DOCK8* gene have been found to cause autosomal recessive hyper-IgE syndrome (AR-HIES), an immune system disorder that causes recurrent severe infections of the skin and respiratory tract. Most of the mutations involved in this disorder delete regions of DNA from the *DOCK8* gene. These deletions and other *DOCK8* gene mutations lead to an abnormally short protein, if any protein is produced. As a result, affected individuals have little or no functional DOCK8 protein.

A shortage of DOCK8 protein impairs normal immune cell development and function. It is thought that T cells lacking DOCK8 cannot maintain their shape as they move through dense spaces, such as those found within the skin. The abnormal cells die, resulting in reduced numbers of these cells. A shortage of T cells impairs the immune response to foreign invaders, accounting for the severe skin infections common in

AR-HIES. A lack of DOCK8 also impairs B cell maturation and the production of antibodies. Impairment of this type of immune response leads to recurrent respiratory tract infections in people with this disorder.

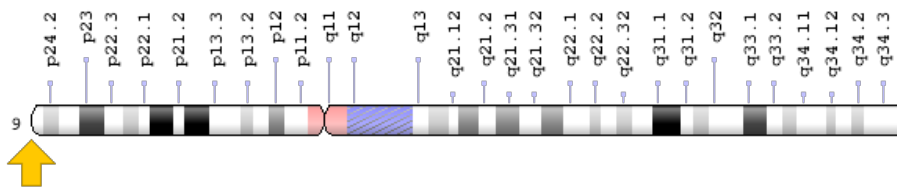
other disorders

Mutations affecting the *DOCK8* gene have been found in two individuals with a rare form of intellectual disability described in the medical literature as autosomal dominant mental retardation 2. These individuals have developmental delays, including delayed or absent speech. The mutations involved in this condition result in production of an abnormally short DOCK8 protein. Unlike in AR-HIES (described above), the mutations associated with autosomal dominant mental retardation 2 affect only one copy of the *DOCK8* gene. Researchers are unsure how these genetic changes lead to intellectual disability.

Chromosomal Location

Cytogenetic Location: 9p24.3, which is the short (p) arm of chromosome 9 at position 24.3

Molecular Location: base pairs 211,297 to 465,260 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- 1200017A24Rik
- dedicator of cytokinesis protein 8 isoform 1
- dedicator of cytokinesis protein 8 isoform 2
- dedicator of cytokinesis protein 8 isoform 3
- epididymis luminal protein 205
- FLJ00026
- FLJ00152
- FLJ00346

- HEL-205
- MRD2
- ZIR8

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): B Cells and Antibodies
<https://www.ncbi.nlm.nih.gov/books/NBK26884/>
- Molecular Biology of the Cell (fourth edition, 2002): Extracellular Signals Can Induce Major Cytoskeletal Rearrangements
https://www.ncbi.nlm.nih.gov/books/NBK26809/#_A3037_
- Molecular Biology of the Cell (fourth edition, 2002): T Cells and MHC Proteins
<https://www.ncbi.nlm.nih.gov/books/NBK26926/>

Genetic Testing Registry

- GTR: Genetic tests for DOCK8
<https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=81704%5Bgeneid%5D>

Scientific articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28DOCK8%5BTIAB%5D%29+OR+%28dedicator+of+cytokinesis+8%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- DEDICATOR OF CYTOKINESIS 8
<http://omim.org/entry/611432>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_DOCK8.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=DOCK8%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=19191

- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/81704>
- UniProt
<http://www.uniprot.org/uniprot/Q8NF50>

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